

**REMARKS**

Claims 1-6, 9-18 and 21-67 are pending in the present application. Claims 6, 10, 15, 18, 22, 27, 29, and 30-61 have been withdrawn from consideration. Claims 1 and 62 have been amended to recite that the VEGFR antibody “specifically binds to VEGFR and inhibits binding of a ligand thereto” and that the EGFR antibody “specifically binds to EGFR and inhibits binding of a ligand thereto.” Support for these claims amendments can be found, *inter alia*, in original claims 7, 8, 19 and 20 (which have therefore been canceled) and in paragraphs 56, 57, 75, 84, and 86 of the present specification. Applicants submit that these claims amendments do not raise new issues or require an additional search since original claims 7, 8, 19, and 20 required the Examiner to address the issue of and perform a search for the claim limitations now present in claims 1 and 62. As such, Applicants submit that these amendments are proper at this stage of prosecution.

Claims 1-5, 7-9, 11-14, 16-17, 19-21, 23-26, 28, 62, and 67 stand rejected under 35 U.S.C. §103(a) as being allegedly rendered obvious by U.S. Patent No. 6,448,077 to Rockwell (the ‘077 patent) in view of Petit *et al.*, “Neutralizing Antibodies Against EGFR and ErbB-2/neu Receptor Tyrosine Kinases Down-Regulated Vascular Endothelial Growth Factor Production by Tumor Cells *in Vitro* and *in Vivo*,” American Journal of Pathology 151(6): 1523-1530 (1997) (“Petit”) as evidenced by Kawamoto *et al.*, American Journal of Pathology 151 (6): 1523-1530 (“Kawamoto”).

As an initial matter, Applicants submit that the ‘077 patent does not qualify as prior art under 35 U.S.C. §103(a). The ‘077 patent issued into a patent on September 10, 2002 but the present application has an actual filing date of March 4, 2002 and claims priority back to an application having a filing date of February 4, 1994.

Pursuant to 35 U.S.C. §103(c), a reference which only qualifies as prior art under 35 U.S.C. §102(e) cannot be used as prior art under 35 U.S.C. §103(a) if the prior art and the application were subject to an obligation of assignment to the same person at the time the claimed invention was made. Here, the ‘077 patent relied on by the Examiner in making this rejection and the present invention were both either assigned or subject to an obligation of assignment to ImClone Systems Incorporated (“ImClone”) at the time the present invention was made and such obligation was later fulfilled (See Reel 012919, Frame 0422 and Reel 008347, Frame 0747). Therefore, the ‘077 patent does not qualify as prior art for §103(a) purposes.

In any event, the present claims are not rendered obvious by any of the other Rockwell patents cited in the Information Disclosure Statement of June 11, 2003 in view of Petit. According to the Examiner, one skilled in the art would be motivated to combine the teaching of Rockwell and Petit because “anti-VEGFR and anti-EGFR antibodies are functional equivalents with respect to inhibiting the interaction between the VEGF receptor and its ligand.” Applicants take issue with this analysis since VEGFR antibodies and EGFR antibodies, as recited by the present claims, do not serve the same function. Specifically, the present claims recite that the VEGFR antibody (or functional equivalent thereof) specifically binds to VEGFR and inhibits binding of a ligand thereto and the EGFR antibody (or functional equivalent thereof) specifically binds to EGFR and inhibits binding of a ligand thereto. Petit in no way describes an EGFR antibody as serving this same function of a VEGFR antibody. Specifically, Petit only describes down-regulation of VEGF production in cancer cells upon treatment with an EGFR antibody. There is no disclosure in Petit of an EGFR antibody inhibiting binding of VEGF to VEGFR, which is encompassed by the recitation in the present claims of a VEGFR antibody inhibiting binding of a ligand to VEGFR.

Further, Applicants submit that there is no motivation to combine the teachings of Rockwell and Petit since Petit shows that administration of an EGFR antibody alone down-regulates VEGF expression and inhibits tumor growth. Specifically, according to Petit’s studies, administration of 4D5 and C225, both EGFR antibodies, results in a dose-dependent decrease in VEGF production (See page 1526). Moreover, administration of C225 alone resulted in “appreciable inhibition of tumor growth” and a “pronounced withdrawal of tumor cells from the cell cycle when the mice were exposed to C225.” (Page 1527). Applicants submit that such disclosure would not motivate one skilled in the art to combine treatment of an EGFR antibody with a VEGFR antibody. Rather, Applicants submit that such disclosure would suggest to one skilled in the art that with EGFR antibody therapy, there is no need for additional treatment with a VEGFR antibody that binds to VEGFR and neutralizes activation thereof as disclosed by Rockwell, or would suggest that such additional treatment is redundant. Therefore, based on the teachings of Petit, one skilled in the art would not be motivated to combine the teachings of Rockwell and Petit to produce a method of inhibiting tumor growth by administering both an EGFR and VEGFR antibody. For at least these reasons, Applicants submit that a *prima facie* case of obviousness has not been established and Applicants request withdrawal of this rejection.

PATENT  
Appl. No. 10/091,300  
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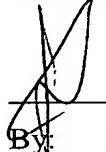
**CONCLUSION**

It is respectfully submitted that the present application is now in condition for allowance, which action is respectfully requested. The Examiner is invited to contact Applicants' representative to discuss any issue that would expedite allowance of the subject application.

Any fees for extension(s) of time or additional fees are required in connection with the filing of this response, such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and the Commissioner is authorized to charge any such required fees or to credit any overpayment to Kenyon & Kenyon's Deposit Account No. 11-0600.

Respectfully submitted,

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